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INDUSTRIAL CHALLENGES FOR QUANTUM CHEMISTRY

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The current fields of application of quantum chemical methods in the chemical industry are described. Although there are a lot of questions that already can be tackled with modern algorithms and computers, there are still important problems left which will need further improved methods. A few examples are given in this article.

1 Introduction

Already in the 1970's and 80's, quantum chemical methods were very successful in describing the structure and properties of organic and main-group inorganic molecules. The Hartree-Fock (HF) method and its simplified semi-empirical modifications became standard tools for a vivid rationalization of chemical processes. The underlying molecular orbital (MO) picture was, and still is, the most important theoretical concept for the interpretation of reactivity and molecular properties. Nevertheless, quantum chemical methods were not used extensively for industrial problems, although most of the industrial chemistry produces organic compounds. One reason can be found in the fact that almost all industrial processes are catalytic. The catalysts are predominantly transition metal compounds, which in general have a more complicated electronic structure than main-group compounds, since their variability in the occupation of the d orbitals results in a subtle balance of several close lying energy levels. HF and post-HF methods based on a single electron configuration are not able to describe this situation correctly. Furthermore, the catalyst systems were generally too big to be handled. The usual approach was to choose small model systems, e.g. with PH3 substituting any phosphine ligand or a cluster representing a solid surface. Such investigations provided only a basic understanding of the catalytic reaction, but no detailed knowledge on steric and electronic dependencies.

With the improvement of both the methodology and the algorithms of density functional theory (DFT) in the last two decades, the situation changed significantly. DFT appears to be less sensitive to near degeneracy of electronic states, and furthermore incorporates some effects of electron correlation. The development of new functionals with improved description of non-uniform electron distributions in molecules or on surfaces, paved the way for a qualitative or even quantitative quantum chemical treatment of a large variety of transition metal compounds and their reactions. When functionals without partial inclusion of HF exchange contributions are used, an approximate treatment of the Coulomb interaction of the electrons (density fitting, resolution of identity (RI) approach) allows for a very ef-

ficient treatment of large systems. Therefore, with efficiently parallelized programs of this kind, it is routinely possible today to calculate the structure of molecules with 100-200 atoms.

Although the chemical processes in many cases involve transition metal compounds, calculations on pure organic molecules are still important to predict properties like thermodynamic data or various types of spectra. However, for a quantitative agreement between calculated and experimental results, DFT very often is not reliable enough, and approaches going beyond the HF approximation are necesary to assess the effects caused by electron correlation. These methods are computationally very demanding, and highly accurate calculations are still limited to small molecules with not more than about 10 atoms. Therefore, still only few problems of industrial relevance can be tackled by these methods at the moment.

2 Application fields of quantum chemistry in industry

2.1 Catalysis

As already mentioned, many of the industrial chemical processes involve catalysts. Most of the catalysts are in the solid state (heterogeneous catalysis), but, with the extensive developments in organometallic chemistry in the last decades, catalytic processes in the liquid phase become more and more important (homogeneous catalysis). For the development of a catalyst, besides economic considerations, three issues are of central importance:

- Activity: The catalyst must be efficient (high turnover numbers).
- Selectivity: By-products should be avoided.
- Stability: Deactivation or decomposition of the catalyst must be slow.

To improve a catalyst with respect to these criteria, a detailed understanding of the reaction pathways is necessary. This is one point, where quantum chemical methods can be of enormous value, since the experimental investigation of steps in a complicated mechanism is rather difficult. Once the crucial parameters are found, new guesses for better performing catalysts can be deduced and immediately be tested in the calculations. Thus, when theory is used for a rough screening and only the most promising candidates have to be tested in experiment, the development process for new catalysts can be shortened significantly. DFT is used almost exclusively for both homogeneous and heterogeneous applications. In the latter case, solids are treated with preriodic boundary conditions or QM/MM approaches.

2.2 Process design

The design of chemical processes and plants requires the knowledge of accurate thermodynamic and kinetic data for all substances and reactions involved. The experimental determination of such data is rather time-consuming and expensive. The substances have to be prepared in high purity and precise calorimetric or kinetic measurements have to be done for well-defined reactions. This effort must

be invested before the actual technical realization of a new process, because for economic and safety reasons, the data has to be as accurate as possible. However, for an early assessment of the practicability and profitability of a process, a fast but nevertheless reliable estimate for the thermodynamics usually is sufficient. A number of empirical methods based on group contributions are used for this purpose, but they are not generally applicable and often not reliable enough. For example, these methods often can not discriminate between isomers containing the same number and type of groups. Alternatively, reaction enthalpies and entropies can also be calculated by quantum chemical methods in combination with statistical mechanics. For the rotational and vibrational energy levels, a correct description of the molecular structure and the shape of the energy surface is needed, which can very efficiently be obtained with DFT. The crucial point for the overall accuracy, however, are the differences in electronic energies, and high level ab initio methods like coupled cluster theories are often needed to get the error down to a few kcal/mol. That such a high accuracy is needed can be illustrated by the fact, that a change in the Gibbs free energy of only 1.4 kcal/mol already changes an equilibrium constant by an order of magnitude at room temperature.

2.3 Material properties

When a desired property of a material can be connected to quantities on the atomic or molecular scale, quantum chemistry can be a useful tool in the process of improving such materials. Typical examples are dyes and pigments, for which color and brilliance depend on the energies and nature of electronic excitations. Organic dyes typically have delocalized pi systems and functional groups chosen appropriately to tune the optical properties. Since the molecules normally are too big for an ab initio treatment with the desired accuracy, semi-empirical methods are currently used to calculate the excited states.

3 Unsolved problems

3.1 Treatment of the molecular environment

Quantum chemical methods are predominantly applied to isolated molecules, which corresponds to the state of an ideal gas. Most chemical processes, however, take place in condensed phase, and the interaction of a molecule with its environment can generally not be neglected. Two important examples are given here.

3.1.1 Solvent effects

Solvent molecules can directly interact with the reacting species, e.g. by coordination to a metal center or by formation of hydrogen bonds. In such cases it is necessary to explicitely include solvent molecules in the calculation. Depending on the size of the solvent molecules and their number needed to get the calculated properties converged, the overall size of the molecular system and the resulting computational effort can significantly be increased. Currently, only semi-empirical methods are able to handle several hundred atoms, but the developments towards

linear scaling approaches in DFT are very promising. An alternative would be a mixed quantum mechanical (QM) and molecular mechanical (MM) treatment (QM/MM method).

If there are no specific solute-solvent interactions, the main effect of the solvent is electrostatic screening, depending on its dielectric constant. This can be described very efficiently by continuum solvation models (CSM).

3.1.2 Enzymes

Biomolecules like enzymes usually consist of many thousands of atoms and therefore can not be handled by quantum chemical methods. Although there exist several very elaborate force field methods which quite reliably reproduce protein structures, the accurate description of the interaction of the active site with a ligand bound to it still is an unsolved problem. Quantum mechanics is needed for a quantitative assessment of polarization effects and for the description of reactions. Treating only the active site quantum mechanically usually does not give the correct results because of the strong electrostatic influence of the whole enzyme and the water molecules included. QM/MM approaches can be used for the treatment of the whole system, but the QM/MM coupling still needs improvement.

A very important quantity of an enzyme/ligand complex is its binding free energy. It determines the measured equilibrium constant for a ligand exchange and is therefore important for the development of enzyme inhibitors. A reliable calculation of such binding constants is currently not possible. It certainly must involve quantum chemistry and molecular dynamics.

3.2 Accurate thermochemistry and kinetics

The highly accurate calculation of thermochemical data with ab initio methods is currently possible only for small molecules up to about 10 atoms. However, many of the data for molecules of this size are already known, whereas accurate experiments for larger compounds are quite rare. Therefore, efficient ab initio methods are needed which are able to treat molecules with 30-50 atoms with the same level of accuracy. The currently developed local treatments of electron correlation are very promising in this direction.

Another problem arises for large molecules. They often have a high torsional flexibility, and the calculation of partition functions based on a single conformer is therefore not correct. Quantum molecular dynamics could probably give better answers, but is in many cases too expensive.

For the assessment of catalytic mechanisms, kinetic data are needed to discriminate between different reaction pathways. As described above, ab initio methods are often not applicable when transition metals are involved. The DFT results for reaction energies are usually reliable enough to give correct trends, but calculated activation barriers easily can be wrong by a factor of two or more. The problem lies in the functionals, which best describe the electron distribution in the molecular ground states.

3.3 Spectroscopy for large molecules

Calculated molecular spectroscopic properties are very helful in the assignment and interpretation of measured spectra, provided that the accuracy is sufficiently high. In many cases IR, Raman and NMR spectra can be obtained with reasonable accuracy on DFT or MP2 level, but UV/VIS spectra normally require more elaborate theories like configuration interaction, which are only applicable to very small molecules. To improve on the currently applied semi-empirical approaches it would be necessary to calculate accurate excitation energies also for, e.g., organic dyes with 50 or even more atoms.

4 Conclusion

The improvement of the efficiency of the algorithms and the enormous increase of the available computer power already made quantum chemistry applicable to a lot of industrial problems. However, there are still many aspects concerning the accuracy, completeness and efficiency of the quantum chemical treatment, which will need more attention in the future.

Currently, DFT is the most widely used quantum theoretical method in industry. Also of high importance are semi-empirical methods for certain applications. Both approaches have in common that they do not offer a systematic way for the improvement of results, if they are found to be not reliable enough. Therefore, there is still need for efficient ab initio methods, at least as a reference.